REMARKS

Status of the Claims

Claims 1-17 are pending in this application. No claims have been canceled or added. Claim 9 has been amended to delete an offensive phrase. Claims 1-3, 9-10 and 16-17 have been amended to delete any overlapping substituents disclosed in the cited references.

Unexpected Superior Results

Applicants also submit that comparative tests demonstrate unexpected superior results of the present invention over 8-methyl-5-(4-aminophenyl)-9H-1,3-dioxolo[4,5-h]-[2,3]-benzodiazepine, compound A of the cited art. Please see comparative pharmacological test data at pages 21-28 of the specification. It is clear that the present invention has superior effects in muscle relaxation, inhibition of maximal electroshock and audiogeneric seizure and global ischemia over the comparative examples.

As such, Applicants submit that the present invention is patentable over the cited art as the present invention has superior and unexpected effects over the prior art compounds.

Conclusion

As Applicants have addressed and overcome all rejections, Applicants respectfully request that the rejections be withdrawn and that the claims be allowed.

Should there be any outstanding matters that need to be resolved in the present application, the Examiner is respectfully requested to contact Kecia Reynolds (Reg. No. 47,021) at the telephone number of the undersigned below, to conduct an interview in an effort to expedite prosecution in connection with the present application.

Attached hereto is a marked-up version of the changes made to the application by this Amendment.

Pursuant to the provisions of 37 C.F.R. § 1.17 and 1.136(a), Applicants hereby petition for an extension of two (2) months to August 18, 1998 for the period in which to file a response to the outstanding Office Action. The required fee of $400.00 is attached hereto.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees required under 37 C.F.R. §§ 1.16 or 1.17; particularly, extension of time fees.

Respectfully submitted,

BIRCH, STEWART, KOLASCH & BIRCH, LLP

By _____
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Attachment: Version with Markings to Show Changes Made

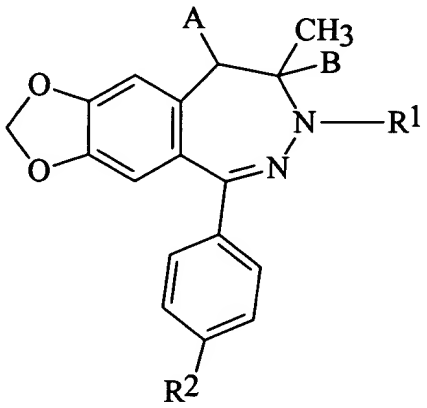
(Rev. 02/20/02)

VERSION WITH MARKINGS TO SHOW CHANGES MADE

IN THE CLAIMS:

The claims have been amended as follows:

1. (Thrice Amended) A 1,3-dioxolo-[4,5-h][2,3]benzodiazepine compound of the formula I



I

wherein

A represents a hydrogen atom,

B means a hydrogen atom,

R^1 stands for a group of the formula

$-(CH_2)_n-CO-(CH_2)_m-R$, wherein

R represents a halo atom, a pyridyl group or a group of the formula $-NR^3R^4$, wherein

R^3 and R^4 mean, independently, a hydrogen atom, a C_{3-6} cycloalkyl group, a C_{1-4} alkoxy group, an amino group, a phenyl group optionally substituted by one or two C_{1-4} alkyl group(s), a

C_{1-4} alkyl group which latter is optionally substituted by a phenyl group or a saturated heterocyclic group having 5 or 6 members and comprising 1 to 3 nitrogen atom(s) or a nitrogen atom and an oxygen atom as the heteroatom, and said heterocyclic group is optionally substituted by a phenyl group which latter is optionally substituted by 1 to 3 substituent(s), wherein the substituent consists of a C_{1-4} alkoxy group, or

R^3 and R^4 form, with the adjacent nitrogen atom and optionally with a further nitrogen atom or an oxygen atom, a saturated or unsaturated heterocyclic group having 5 or 6 members, being optionally substituted by a phenyl group that is optionally substituted by 1 to 3 substituents, wherein the substituent is a C_{1-4} alkoxy group,

n has a value of 0, 1 or 2,

m has a value of 0, 1 or 2, or

A forms together with B a valence bond between the carbon atoms in positions 8 and 9, and in this case

R^1 represents a group of the formula

$-CO-(CH_2)_p-R^6$, wherein

R^6 stands for a halo atom, a phenoxy group, a C_{1-4} alkoxy group or a group of the formula $-NR^7R^8$, wherein

R^7 and R^8 mean, independently, a hydrogen atom, a guanyl group, a C_{3-6} cycloalkyl group or a C_{1-4} alkyl group which latter is optionally substituted by a phenyl group or a saturated heterocyclic group having 5 or 6 members and comprising one or more nitrogen atom(s) or a nitrogen and an oxygen atom as the heteroatom, wherein the phenyl group is optionally substituted by 1 to 3 identical or different substituent(s), wherein the substituent is a C_{1-4} alkoxy group, or

R^7 and R^8 form together with the adjacent nitrogen atom, an oxopyrrolidinyl group, a phthalimido group, or a saturated heterocyclic group having 5 or 6 members and comprising one or more nitrogen atom(s) or a nitrogen and an oxygen atom as the heteroatom, and said heterocyclic group is optionally substituted by 1 to 3 identical or different substituent(s) selected from the group consisting of a hydroxy group, a phenyl group,

a phenoxy group, a phenyl(C_{1-4} alkyl) group or a phenoxy(C_{1-4} alkyl) group, wherein in case of the substituents listed the phenyl or phenoxy group is optionally substituted by 1 to 3 identical or different substituent(s), wherein the substituent is a halo atom or a C_{1-4} alkoxy group, and, in case of the phenoxy(C_{1-4} alkyl) group, the alkyl group is optionally substituted by 1 or 2 hydroxy group(s),

p has a value of 0, 1 or 2,

R^2 stands for a nitro group, an amino group or a (C_{1-4} alkanoyl)amino group, with the proviso that

1) if A forms together with B a valence bond, R^2 stands for a nitro group or an amino group and p has a value of 0, then R^6 is different from a C_{1-4} alkoxy group,

2) if A forms together with B a valence bond, R^2 stands for a nitro group or an amino group, p has a value of 0 or 1, and R^6 represents a group of the formula $-NR^7R^8$, then one of R^7 and R^8 is different from a hydrogen atom or a C_{1-4} alkyl group,

3) if each of A and B stands for a hydrogen atom, n and m have a value of 0, then one of R^3 and

R^4 represents a hydrogen atom, and the other of R^3 and R^4 is different from a hydrogen atom, a phenyl group or a C_{1-4} alkyl group, and

4) if each of A and B stands for a hydrogen atom, n has a value of 0, m has a value of 1 or 2, and one of R^3 and R^4 stands for a hydrogen atom or a C_{1-14} alkyl group, then the other of R^3 and R^4 is different from a hydrogen atom or a C_{1-4} alkyl group,

5) R is other than a chlorine atom; and with the further proviso that

6) R^3 and R^4 cannot form with the adjacent nitrogen atom a pyrrolidine group,

and pharmaceutically suitable acid addition salts thereof.

2. (Twice Amended) A 1,3-dioxolo-[4,5-h][2,3] benzodiazepine compound as claimed in Claim 1, wherein

A represents a hydrogen atom,

B means a hydrogen atom,

R^1 stands for a group of the formula

$-(CH_2)_n-CO-(CH_2)_m-R$, wherein

R represents a [chloro atom, a] pyridyl group or a group of the formula $-NR^3R^4$, wherein

R^3 and R^4 mean, independently, a hydrogen atom, a cyclopropyl group, a C_{1-4} alkoxy group, an amino group, a phenyl group optionally substituted by one or two methyl group(s), or a C_{1-4} alkyl group which latter is optionally substituted by a phenyl group or a saturated heterocyclic group having 5 or 6 members and comprising 1 to 3 nitrogen atom(s) or a nitrogen atom and an oxygen atom as the heteroatom, and the heterocyclic group is optionally substituted by a phenyl group which latter is optionally substituted by 1 to 3 methoxy groups, or

R^3 and R^4 form, with the adjacent nitrogen atom and optionally with a further nitrogen atom or an oxygen atom, a saturated or unsaturated heterocyclic group having 5 or 6 members, being optionally substituted by a phenyl group that is optionally substituted by 1 to 3 methoxy groups,

n has a value of 0, 1 or 2,

m has a value of 0, 1 or 2,

R^2 stands for a nitro group or an amino group, with the proviso that

1) if n and m have a value of 0, then one of R^3 and R^4 represents a hydrogen atom, and the

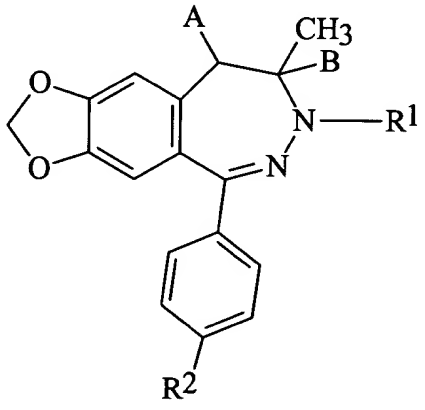
other of R^3 and R^4 is different from a hydrogen atom, a phenyl group or a C_{1-4} alkyl group, [and]

2) if n has a value of 0, m has a value of 1 or 2, and one of R^3 and R^4 stands for a hydrogen atom or a C_{1-4} alkyl group, then the other of R^3 and R^4 is different from a hydrogen atom or a C_{1-4} alkyl group, and

3) R^3 and R^4 cannot form with the adjacent nitrogen atom a pyrrolidine group,

and pharmaceutically suitable acid addition salts thereof.

9. (Twice Amended) A pharmaceutical composition comprising a 1,3-dioxolo-[4,5-h][2,3]benzodiazepine compound of the formula I



I

wherein

A represents a hydrogen atom,

B means a hydrogen atom,

R^1 stands for a group of the formula

$-(CH_2)_n-CO-(CH_2)_m-R$, wherein

R represents a halo atom, a pyridyl group or a group of the formula $-NR^3R^4$, wherein

R^3 and R^4 mean, independently, a hydrogen atom, a C_{3-6} cycloalkyl group, a C_{1-4} alkoxy group, an amino group, a phenyl group optionally substituted by one or two C_{1-4} alkyl group(s), a C_{1-4} alkyl group which is optionally substituted by a phenyl group or a saturated heterocyclic group having 5 or 6 members and comprising 1 to 3 nitrogen atom(s) or a nitrogen atom and an oxygen atom as the heteroatom, and said heterocyclic group is optionally substituted by a phenyl group which is optionally substituted by 1 to 3 substituent(s), wherein the substituent consists of a C_{1-4} alkoxy group, or

R^3 and R^4 form, with the adjacent nitrogen atom and optionally with a further nitrogen atom or an oxygen atom, a saturated or unsaturated heterocyclic group having 5 or 6 members, being optionally substituted by a phenyl group that is

optionally substituted by 1 to 3 substituents, wherein the substituent is a C_{1-4} alkoxy group,

n has a value of 0, 1 or 2,

m has a value of 0, 1 or 2, or

A forms together with B a valence bond between the carbon atoms in positions 8 and 9, and in this case

R^1 represents a group of the formula

$-CO-(CH_2)_p-R^6$, wherein

R^6 stands for a halo atom, a phenoxy group, a C_{1-4} alkoxy group or a group of the formula $-NR^7R^8$, wherein

R^7 and R^8 mean, independently, a hydrogen atom, a guanyl group, a C_{3-6} cycloalkyl group or a C_{1-4} alkyl group which latter is optionally substituted by a phenyl group or a saturated heterocyclic group having 5 or 6 members and comprising one or more nitrogen atom(s) or a nitrogen and an oxygen atom as the heteroatom, wherein the phenyl group is optionally substituted by 1 to 3 identical or different substituent(s), wherein the substituent is a C_{1-4} alkoxy group, or

R^7 and R^8 form together with the adjacent nitrogen atom, an oxopyrrolidinyl group, a phthalimido

group which [latter] is optionally substituted, or a saturated heterocyclic group having 5 or 6 members and comprising one or more nitrogen atom(s) or a nitrogen and an oxygen atom as the heteroatom, and said heterocyclic group is optionally substituted by 1 to 3 identical or different substituent(s) selected from the group consisting of a hydroxy group, a phenyl group, a phenoxy group, a phenyl(C_{1-4} alkyl) group or a phenoxy(C_{1-4} alkyl) group, wherein in case of the substituents listed the phenyl or phenoxy group is optionally substituted by 1 to 3 identical or different substituent(s), wherein the substituent is a halo atom or a C_{1-4} alkoxy group, and, in case of the phenoxy(C_{1-4} alkyl) group, the alkyl group is optionally substituted by 1 or 2 hydroxy group(s),

p has a value of 0, 1 or 2,

R^2 stands for a nitro group, an amino group or a (C_{1-4} alkanoyl)amino group, with the proviso that

1) if A forms together with B a valence bond, R^2 stands for a nitro group or an amino group and

p has a value of 0, then R^6 is different from a C_{1-4} alkoxy group,

2) if A forms together with B a valence bond, R^2 stands for a nitro group or an amino group, p has a value of 0 or 1, and R^6 represents a group of the formula $-NR^7R^8$, then one of R^7 and R^8 is different from a hydrogen atom or a C_{1-4} alkyl group,

3) if each of A and B stands for a hydrogen atom, n and m have a value of 0, then one of R^3 and R^4 represents a hydrogen atom, and the other of R^3 and R^4 is different from a hydrogen atom, a phenyl group or a C_{1-4} alkyl group, [and]

4) if each of A and B stands for a hydrogen atom, n has a value of 0, m has a value of 1 or 2, and one of R^3 and R^4 stands for a hydrogen atom or a C_{1-4} alkyl group, then the other of R^3 and R^4 is different from a hydrogen atom or a C_{1-14} alkyl group, and

5) R^3 and R^4 cannot form with the adjacent nitrogen atom a pyrrolidine group,

or a pharmaceutically suitable acid addition salt thereof as the active ingredient and one or more conventional carrier(s).

10. (Thrice Amended) A pharmaceutical composition as claimed in Claim 9 comprising a 1,3-dioxolo-[4,5-h][2,3]benzodiazepine compound of the formula I, wherein

A represents a hydrogen atom,

B means a hydrogen atom,

R^1 stands for a group of the formula

$-(CH_2)_n-CO-(CH_2)_m-R$, wherein

R represents a [chloro atom, a] pyridyl group or a group of the formula $-NR^3R^4$, wherein

R^3 and R^4 mean, independently, a hydrogen atom, a cyclopropyl group, a C_{1-4} alkoxy group, an amino group, a phenyl group optionally substituted by one or two methyl group(s), or a C_{1-4} alkyl group which latter is optionally substituted by a phenyl group or a saturated heterocyclic group having 5 or 6 members and comprising 1 to 3 nitrogen atom(s) or a nitrogen atom and an oxygen atom as the heteroatom, and said heterocyclic group is optionally substituted by a phenyl group

which latter is optionally substituted by 1 to 3 methoxy groups, or

R^3 and R^4 form, with the adjacent nitrogen atom and optionally with a further nitrogen atom or an oxygen atom, a saturated or unsaturated heterocyclic group having 5 or 6 members, being optionally substituted by a phenyl group that is optionally substituted by 1 to 3 methoxy groups,

n has a value of 0, 1 or 2,

m has a value of 0, 1 or 2,

R^2 stands for a nitro group or an amino group, with the proviso that

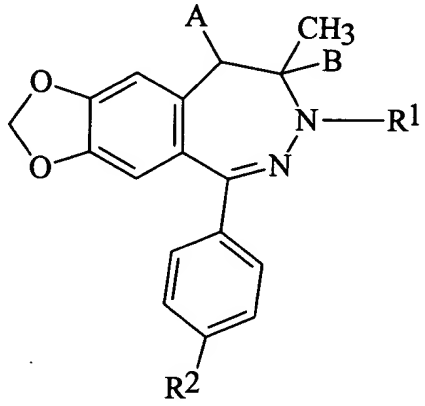
1) if n and m have a value of 0, then one of R^3 and R^4 represents a hydrogen atom, and the other of R^3 and R^4 is different from a hydrogen atom, a phenyl group or a C_{1-4} alkyl group, [and]

2) if n has a value of 0, m has a value of 1 or 2, and one of R^3 and R^4 stands for a hydrogen atom or a C_{1-4} alkyl group, then the other of R^3 and R^4 is different from a hydrogen atom or a C_{1-4} alkyl group, and

3) R^3 and R^4 cannot form with the adjacent nitrogen atom a pyrrolidine group,

or a pharmaceutically suitable acid addition salt thereof as the active ingredient.

16. (Thrice Amended) A method of treatment in which a patient suffering from epilepsy or being in a state after stroke is treated with a non-toxic dose of a 1,3-dioxolo-[4,5-h][2,3]benzodiazepine compound of the formula I,



I

wherein

A represents a hydrogen atom,

B means a hydrogen atom,

R^1 stands for a group of the formula

$-(CH_2)_n-CO-(CH_2)_m-R$, wherein

R represents a halo atom, a pyridyl group or a group of the formula $-NR^3R^4$, wherein

R^3 and R^4 mean, independently, a hydrogen atom, a C_{3-6} cycloalkyl group, a C_{1-4} alkoxy group, an amino group, a phenyl group optionally

substituted by one or two C_{1-4} alkyl group(s), a C_{1-4} alkyl group which latter is optionally substituted by a phenyl group or a saturated heterocyclic group having 5 or 6 members and comprising 1 to 3 nitrogen atom(s) or a nitrogen atom and an oxygen atom as the heteroatom, and said heterocyclic group is optionally substituted by a phenyl group which latter is optionally substituted by 1 to 3 substituent(s), wherein the substituent consists of a C_{1-4} alkoxy group, or

R^3 and R^4 form, with the adjacent nitrogen atom and optionally with a further nitrogen atom or an oxygen atom, a saturated or unsaturated heterocyclic group having 5 or 6 members, being optionally substituted by a phenyl group that is optionally substituted by 1 to 3 substituents, wherein the substituent is a C_{1-4} alkoxy group,

n has a value of 0, 1 or 2,

m has a value of 0, 1 or 2, or

A forms together with B a valence bond between the carbon atoms in positions 8 and 9, and in this case

R^1 represents a group of the formula

$-CO-(CH_2)_p-R^6$, wherein

R^6 stands for a halo atom, a phenoxy group, a C_{1-4} alkoxy group or a group of the formula $-NR^7R^8$, wherein

R^7 and R^8 mean, independently, a hydrogen atom, a guanyl group, a C_{3-6} cycloalkyl group or a C_{1-4} alkyl group which latter is optionally substituted by a phenyl group or a saturated heterocyclic group having 5 or 6 members and comprising one or more nitrogen atom(s) or a nitrogen and an oxygen atom as the heteroatom, wherein the phenyl group is optionally substituted by 1 to 3 identical or different substituent(s), wherein the substituent is a C_{1-4} alkoxy group, or

R^7 and R^8 form together with the adjacent nitrogen atom, an oxopyrrolidinyl group, a phthalimido group, or a saturated heterocyclic group having 5 or 6 members and comprising one or more nitrogen atom(s) or a nitrogen and an oxygen atom as the heteroatom, and said heterocyclic group is optionally substituted by 1 to 3 identical or different substituent(s) selected from the group consisting of a hydroxy group, a phenyl group,

a phenoxy group, a phenyl(C_{1-4} alkyl) group or a phenoxy(C_{1-4} alkyl) group, wherein in case of the substituents listed the phenyl or phenoxy group is optionally substituted by 1 to 3 identical or different substituent(s), wherein the substituent is a halo atom or a C_{1-4} alkoxy group, and, in case of the phenoxy(C_{1-4} alkyl) group, the alkyl group is optionally substituted by 1 or 2 hydroxy group(s),

p has a value of 0, 1 or 2,

R^2 stands for a nitro group, an amino group or a (C_{1-4} alkanoyl)amino group, with the proviso that

1) if A forms together with B a valence bond, R^2 stands for a nitro group or an amino group and p has a value of 0, then R^6 is different from a C_{1-4} alkoxy group,

2) if A forms together with B a valence bond, R^2 stands for a nitro group or an amino group, p has a value of 0 or 1, and R^6 represents a group of the formula $-NR^7R^8$, then one of R^7 and R^8 is different from a hydrogen atom or a C_{1-4} alkyl group,

3) if each of A and B stands for a hydrogen atom, n and m have a value of 0, then one of R^3 and R^4 represents a hydrogen atom, and the other of R^3 and R^4 is different from a hydrogen atom, a phenyl group or a C_{1-14} alkyl group, [and]

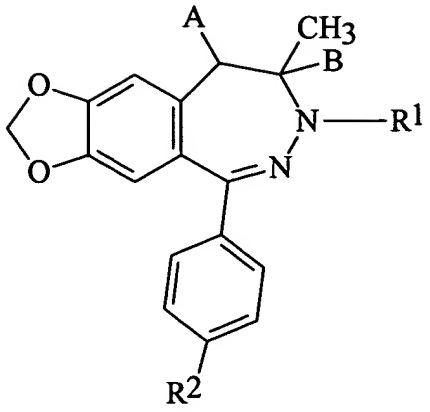
4) if each of A and B stands for a hydrogen atom, n has a value of 0, m has a value of 1 or 2, and one of R^3 and R^4 stands for a hydrogen atom or a C_{1-14} alkyl group, then the other of R^3 and R^4 is different from a hydrogen atom or a C_{1-4} alkyl group,

5) R^3 and R^4 cannot form with the adjacent nitrogen atom a pyrrolidine group, and

6) R^6 is other than a chlorine atom;

or a pharmaceutically suitable acid addition salt thereof.

17. (Thrice Amended) A process for preparing a pharmaceutical composition suitable for the treatment of epilepsy or a state after stroke, characterized in that a 1,3-dioxolo-[4,5-h][2,3]benzodiazepine compound of the formula I,



I

wherein

A represents a hydrogen atom,

B means a hydrogen atom,

R^1 stands for a group of the formula

$-(CH_2)_n-CO-(CH_2)_m-R$, wherein

R represents a halo atom, a pyridyl group or a group of the formula $-NR^3R^4$, wherein

R^3 and R^4 mean, independently, a hydrogen atom, a C_{3-6} cycloalkyl group, a C_{1-4} alkoxy group, an amino group, a phenyl group optionally substituted by one or two C_{1-4} alkyl group(s), a C_{1-4} alkyl group which latter is optionally substituted by a phenyl group or a saturated heterocyclic group having 5 or 6 members and comprising 1 to 3 nitrogen atom(s) or a nitrogen atom and an oxygen atom as the heteroatom, and said heterocyclic group is optionally substituted

by a phenyl group which latter is optionally substituted by 1 to 3 substituent(s), wherein the substituent consists of a C_{1-4} alkoxy group, or

R^3 and R^4 form, with the adjacent nitrogen atom and optionally with a further nitrogen atom or an oxygen atom, a saturated or unsaturated heterocyclic group having 5 or 6 members, being optionally substituted by a phenyl group that is optionally substituted by 1 to 3 substituents, wherein the substituent is a C_{1-4} alkoxy group,

n has a value of 0, 1 or 2,

m has a value of 0, 1 or 2, or

A forms together with B a valence bond between the carbon atoms in positions 8 and 9, and in this case

R^1 represents a group of the formula

$-CO-(CH_2)_p-R^6$, wherein

R^6 stands for a halo atom, a phenoxy group, a C_{1-4} alkoxy group or a group of the formula $-NR^7R^8$, wherein

R^7 and R^8 mean, independently, a hydrogen atom, a guanyl group, a C_{3-6} cycloalkyl group or a C_{1-4} alkyl group which latter is optionally substituted by a phenyl group or a saturated heterocyclic group having 5 or 6 members and

comprising one or more nitrogen atom(s) or a nitrogen and an oxygen atom as the heteroatom, wherein the phenyl group is optionally substituted by 1 to 3 identical or different substituent(s), wherein the substituent is a C_{1-4} alkoxy group, or

R^7 and R^8 form together with the adjacent nitrogen atom, an oxopyrrolidinyl group, a phthalimido group, or a saturated heterocyclic group having 5 or 6 members and comprising one or more nitrogen atom(s) or a nitrogen and an oxygen atom as the heteroatom, and said heterocyclic group is optionally substituted by 1 to 3 identical or different substituent(s) selected from the group consisting of a hydroxy group, a phenyl group, a phenoxy group, a phenyl(C_{1-4} alkyl) group or a phenoxy(C_{1-4} alkyl) group, wherein in case of the substituents listed the phenyl or phenoxy group is optionally substituted by 1 to 3 identical or different substituent(s), wherein the substituent is a halo atom or a C_{1-4} alkoxy group, and, in case of the phenoxy(C_{1-4} alkyl)

group, the alkyl group is optionally substituted by 1 or 2 hydroxy group(s),

p has a value of 0, 1 or 2,

R^2 stands for a nitro group, an amino group or a (C_{1-4} alkanoyl)amino group, with the proviso that

1) if A forms together with B a valence bond, R^2 stands for a nitro group or an amino group and p has a value of 0, then R^6 is different from a C_{1-4} alkoxy group,

2) if A forms together with B a valence bond, R^2 stands for a nitro group or an amino group, p has a value of 0 or 1, and R^6 represents a group of the formula $-NR^7R^8$, then one of R^7 and R^8 is different from a hydrogen atom or a C_{1-4} alkyl group,

3) if each of A and B stands for a hydrogen atom, n and m have a value of 0, then one of R^3 and R^4 represents a hydrogen atom, and the other of R^3 and R^4 is different from a hydrogen atom, a phenyl group or a C_{1-14} alkyl group, [and]

4) if each of A and B stands for a hydrogen atom, n has a value of 0, m has a value of 1 or 2, and one of R^3 and R^4 stands for a

hydrogen atom or a C_{1-4} alkyl group, then the other of R^3 and R^4 is different from a hydrogen atom or a C_{1-4} alkyl group,

5) R is other than a chlorine atom; and with the further proviso that

6) R^3 and R^4 cannot form with the adjacent nitrogen atom a pyrrolidine group,

or a pharmaceutically suitable acid addition salt thereof, together with one or more conventional carrier(s), is converted to a pharmaceutical composition.